

On page 83, line 24, please insert after "Substance P-NH2", --(SEQ ID NO. 112)--.

On page 83, line 24, please insert after "(Lys)6-Substance P-NH2", --(SEQ ID NO. 113)-

On page 83, line 25, please insert after "Substance P-NH2", --(SEQ ID NO. 112)--.

On page 83, line 25, please insert after "(Lys)6-Substance P-NH2", --(SEQ ID NO. 113)-

On page 83, line 9, please insert after "Substance P-NH2", --(SEQ ID NO. 112)--.

On page 83, line 9, please delete "(Lys)6-SubstanceP-NH2" and insert in its place, -- ((Lys)6-SubstanceP-NH₂) (SEQ ID NO. 113)--.

IN THE CLAIMS

Please amend claims 11, 12, 15, 18, 19, 24, and 25 as follows:

- 11. (amended) A peptide conjugate according to claim 10, wherein Z is Lys4 (SEQ ID NO. 55), Lys5 (SEQ ID NO. 56) or Lys6 (SEQ ID NO. 62).
- 12. (amended) A peptide conjugate according to claim 11, wherein Z is Lys6 (SEQ ID NO. 62).
- 15. (amended) A peptide conjugate according to claim 14, wherein Z is (Lys-Glu)3 (SEQ ID NO. 84) or (Glu-Lys)3 (SEQ ID NO. 85).
 - 18. (amended) A peptide conjugate according to claim 17, wherein Z is Lys3-Glu3 (SEQ ID NO. 86) or Glu3-Lys3 (SEQ ID NO. 87).

Lys-Lys-Xaa, Xaa-Xaa-Lys-Lys, Xaa-Lys-Xaa-Lys, Xaa-Lys-Xaa, Lys-Xaa-Xaa-Lys, Lys-Xaa-Lys-Xaa, Lys-Lys-Xaa-Xaa-Xaa-Xaa-Lys, Xaa-Xaa-Lys-Xaa, Xaa-Lys-Xaa-Xaa, Lys-Xaa-Xaa-Xaa, Xaa-Xaa-Xaa, Lys-Lys-Lys-Lys-Lys (SEO ID NO. 56), Xaa-Lys-Lys-Lys (SEQ ID NO. 57), Lys-Xaa-Lys-Lys (SEQ ID NO. 58), Lys-Lys-Xaa-Lys-Lys (SEQ ID NO. 59), Lys-Lys-Lys-Xaa-Lys (SEQ ID NO. 60), Lys-Lys-Lys-Lys-Xaa (SEQ ID NO. 61), Xaa-Xaa-Lys-Lys-Lys, Xaa-Lys-Lys-Lys-Lys-Lys-Xaa, Lys-Lys-Xaa-Xaa-Lys, Lys-Lys-Xaa-Lys-Xaa, Lys-Lys-Lys-Xaa-Xaa, Lys-Lys-Xaa-Xaa-Xaa, Lys-Xaa-Lys-Xaa-Xaa, Lys-Xaa-Lys-Xaa, Lys-Xaa-Xaa-Lys, Xaa-Lys-Lys-Xaa-Xaa, Xaa-Lys-Xaa-Xaa-Lys, Xaa-Xaa-Lys-Lys-Xaa, Xaa-Xaa-Lys-Xaa-Xaa-Xaa, Xaa-Xaa-Xaa-Xaa, Xaa-Xaa-Xaa-Xaa-Xaa-Xaa-Xaa, Lys-Lys-Lys-Lys-Lys-Lys (SEQ ID NO. 62), Xaa-Lys-Lys-Lys-Lys (SEQ ID NO. 63), Lys-Xaa-Lys-Lys-Lys-Lys (SEQ ID NO. 64), Lys-Lys-Lys-Lys-Lys (SEQ ID NO. 65), Lys-Lys-Lys-Xaa-Lys-Lys (SEQ ID NO. 66), Lys-Lys-Lys-Lys-Xaa-Lys (SEQ ID NO. 67), Lys-Lys-Lys-Lys-Lys-Xaa (SEO ID NO. 68), Xaa-Xaa-Lys-Lys-Lys-Lys (SEO ID NO. 69), Xaa-Lys-Xaa-Lys-Lys (SEQ/ID NO. 70), Xaa-Lys-Lys-Xaa-Lys-Lys (SEQ ID NO. 71), Xaa-Lys-Lys-Lys-Xaa-Lys (SEQ ID NO. 72), Xaa-Lys-Lys-Lys-Xaa (SEQ ID NO. 73), Lys-Xaa-Xaa-Lys-Lys-Lys (SEQ ID NO. 74), Lys-Xaa-Lys-Xaa-Lys-Lys (SEQ ID NO. 75), Lys-Xaa-Lys-Lys-Xaa-Lys (SEQ ID NO. 76), Lys-Xaa-Lys-Lys-Lys-Xaa (SEQ ID NO. 77), Lys-Lys-Xaa-Xaa-Lys-Lys (SEQ ID NO. 78), Lys-Lys-Xaa-Lys-Xaa-Lys (SEQ ID NO. 79), Lys-Lys-Xaa-Lys-Lys-Xaa (SEQ ID NO. 80), Lys-Lys-Lys-Xaa-Xaa-Lys (SEQ ID NO. 81), Lys-Lys-Lys-Xaa (SEQ ID NO. 82), Lys-Lys-Lys-Lys-Xaa-Xaa (SEQ ID NO. 83), Xaa-Xaa-Xaa-Lys-Lys-Lys, Xaa-Xaa-Lys-Xaa-Lys-Lys, Xaa-Xaa-Lys-Lys-Xaa-Lys, Xaa-Xaa-Lys-Lys-Lys-Xaa, Xaa-Lys-Xaa-Xaa-Lys-Lys, Xaa-Lys-Xaa-Lys-Xaa-Lys-Xaa-Lys-Xaa-Lys-Xaa-Lys-Xaa-Lys-Xaa-Lys, Xaa-Lys-Lys-Xaa-Lys-Xaa, Xaa-Lys-Lys-Lys-Xaa-Xaa, Lys-Lys-Lys-Xaa-Xaa, Lys-Lys-Xaa-Lys-Xaa-Xaa, Lys-Lys-Xaa-Lys-Xaa, Lys-Lys-Xaa-Xaa-Xaa-Lys, Lys-Xaa-Lys-Lys-Xaa-Xaa, Lys-Xaa-Lys-Xaa-Lys-Xaa, Lys-Xaa-Lys-Xaa-Xaa-Lys, Lys-Xaa-Xaa-Lys-Lys-Xaa, Lys-Xaa-Xaa-Lys-Xaa-Lys, Lys-Xaa-Xaa-Xaa-Lys-Lys, Lys-Lys-Xaa-Xaa-Xaa-Xaa, Lys-Xaa-Lys-Xaa-Xaa, Lys-Xaa-Xaa, Lys-Xaa-Xaa-Lys-

$$-NH-C(R^1)(R^2)-C(=O)-$$

(I)

wherein R¹ and R² are selected from the group consisting of hydrogen, C₁₋₆-alkyl, phenyl, and phenyl-methyl, wherein C₁₋₆-alkyl is optionally substituted with from one to three substituents selected from halogen, hydroxy, amino, cyano nitro, sulfono, and carboxy, and phenyl and phenyl-methyl is optionally substituted with from one to three substituents selected from C₁₋₆-alkyl, C₂₋₆-alkenyl, halogen, hydroxy, amino, cyano, nitro, sulfono, and carboxy, or R¹ and R² together with the carbon atom to which they are bound form a cyclopentyl, cyclohexyl, or cycloheptyl ring, e.g. 2,4-diaminobutancic acid (Dab) and 2,3-diaminopropanoic acid (Dapa).

Subar

24. (amended) The peptide conjugate according to claim 16, wherein X is selected from the group consisting of enkephalin, Leu-enkephalin, Met-enkephalin, angiotensin I, angiotensin II, vasopressin, endothelin, vasoactive intestinal peptide, substance P, neurotensin, endorphins, insulin, gramicidin, paracelsin, delta-sleep inducing peptide, Gonadotropin-Releasing hormone, human parathyroid hormone (1-34), truncated erythropoietin analogues, specifically EMP-1, Atrial natriuretic peptide (ANP, ANF), human brain natriuretic peptide (hBNP), cecropin, kinetensin, neurophysins, elafin, guamerin, attiopeptin I, atriopeptin II, atriopeptin III, deltorphin II, vasotocin, bradykinin, dynorphin, dynorphin A, dynorphin B, growth hormone release factor, growth hormone, growth hormone releasing peptide, oxytocin, calcitonin, calcitonin gene-related peptide, calcitonin gene-related peptide II, growth hormone releasing peptide, tachykinin, adrenocorticotropic hormone (ACTH), brain natriuretic polypeptide,

cholecystokinin, corticotropin releasing factor, diazepam binding inhibitor fragment, FMRFamide, galanin, gastric releasing polypeptide, gastric inhibitory polypeptide, gastrin, gastrin releasing peptide, glucagon, glucagon-like peptide-1, glucagon-like peptide-2, LHRH, melanin concentrating hormone, melanocyte stimulating hormone (MSH), alpha-MSH, morphine modulating peptides, motilin, neurokinin A, neurokinin B, neuromedin B, neuromedin C, neuromedin K, neuromedin N, neuromedin U, neuropeptide K, neuropeptide Y, pituitary adenylate cyclase activating polypeptide (PACAP), pancreatic polypeptide, peptide YY, peptide histidine-methionine amide (PHM), secretin, somatostatin, substance K, , thyrotropinreleasing hormone (TRH), kyotorphin, melanostatin (MIF-1), thrombopoeitin analogs, in particular AF 12505 (Ile-Glu-Gly-Pro-Thr-Leu-Arg-Gln-Trp-Leú-Ala-Ala-Arg-Ala) (SEQ ID NO. 14), insulin-like growth factor I (57-70) (Ala-Leu-Leu-Glu-Thr-Tyr-Cys-Ala-Thr-Pro-Ala-Lys-Ser-Glu) (SEQ ID NO. 15), [insulin-like growth factor J(30-41)] insulin-like growth factor I(30-41) (Gly-Tyr-Gly-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO. 16), insulin-like growth factor I(24-41)(Tyr-Phe-Asn-Lys-Pro-Thr-Gly-Tyr-Gly-Ser-Ser-Arg-Arg-Ala-Pro-Gln-Thr) (SEQ ID NO. 17), insulin-like growth factor II (33-40) (Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO. 18), insulin-like growth [tyro] factor II (33-40) (Tyr-Ser-Arg-Val-Ser-Arg-Arg-Ser-Arg) (SEQ ID NO. 19), insulin-like growth factor II (69-84) [Asp-Val-Ser-Thr-Pro-Pro-Thr-Val-Leu-Pro-Asp-Asn-Phe-Pro-Arg-Tyr)] Asp-Val-Ser-Thr-Pro-Pro-Thr-Val-Leu-Pro-Asp-Asn-Phe-Pro-Arg-Tyr) (SEQ ID NO. 20), growth hormone (GH)-releasing peptide-6 (GHRP-6) [(His-DTrp-Ala-Trp-DPhe-Lys-NH2)] (His-DTrp-Ala-Trp-DPhe-Lys-NH2) (SEQ ID NO. 21), beta-Interleukin I (163-171) (Vál-Gln-Gly-Glu-Glu-Ser-Asn-Asp-Lys) (SEQ ID NO. 22), beta-Interleukin II (44-56) (Ile-Léu-Asn-Gly-Ile-Asn-Asn-Tyr-Lys-Asn-Pro-Lys-Leu) (SEQ ID NO. 23), Interleukin II (60-70) (Leu-Thr-Phe-Lys-Phe-Tyr-Met-Pro-Lys-Lys-Ala) (SEQ ID NO. 24), exendin-4 (GLP-1 analog) [(His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH2)] (His-Gly-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg/Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser-NH2) (SEQ ID NO. 25), exendin-3 (GLP-1 analog) (His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-Asp-Leu-Ser-Lys-Gln-Met-Glu-Glu-Glu-Ala-Val-Arg-Leu-Phe-Ile-Glu-Trp-Leu-Lys-Asn-Gly-Gly-Pro-Ser-Ser-Gly-Ala-Pro-Pro-Pro-Ser) (SEQ ID NO. 26),

[Cys(Acm)20,31] epidermal growth factor (20-31) Cys(Acm)-Met-His-Ile-Glu-Ser-Leu-Asp-Ser-Tyr-Thr-Cys(Acm) (SEQ ID NO. 27), bivalirudin (Hirulog) [(D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu)] (D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Glu-Tyr-Leu) (SEQ ID NO. 28), hirulog-1 D-Phe-Pro-Arg-Pro-(Gly)4-Asn-Gly-Asp-Phe-Glu-Glu-Ile-Pro-Glu-Tyr-Leu (SEQ ID NO. 29), C-type natriuretic peptide (1-53) (CNP) (Asp-Leu-Arg-Val-Asp-Thr-Lys-Ser-Arg-Ala-Ala-Arg-Leu-Leu-Gln-Glu-His-Pro-Asn-Ala-Arg-Lys-Tyr-Lys-Gly-Ala-Asn-Lys-Lys-Gly-Leu-Ser-Lys-Gly-Cys-Phe-Gly-Leu-Lys-Leu-Asp-Arg-Ile-Gly-Ser-Met-Ser-Gly-Leu-Gly-Cys; Disulfide bridge: Cys37-Cys53) (SEQ ID NO. 30), "Mini ANP" (Met-Cys-His-cyclohexylAla-Gly-Gly-Arg-Met-Asp-Arg-Ile-Ser-Cys-Tyr-Argü disulfide bridge cys2-cys13) (SEQ ID NO. 31), Melanotan-II (also known as MT-II, alpha-MSH4-10-NH2, or Ac-Nie4-Asp5-His6-D-Phe7-Arg8-Trp9-Lys10) (SEQ ID NO. 32), thymosin alpha1 (TA1) (Ac-Ser-Asp-Ala-Ala-Val-Asp-Thr-Ser-Ser-Glu-Ile-Thr-Thr-Lys-Asp-Leu-Lys-Glu-Lys-Lys-Glu-Val-Val-Glu-Glu-Glu-Ala-Glu-Asn) (SEQ ID NO. 33), ornipressin (also known as 8-ornithine-vasopressin, (POR-8),

Phe2,Ile3,Orn8]vasopressin), Cys-Phe-Ile-Gln-Asn-Cys-Pro-Orn-Gly-NH2, Disulfide bridge: (ys1-Cys6) (SEQ ID NO. 34), octreotide (20/1-995) (DPhe-Cys-Phe-DTrp-Lys-Thr-Cys-Thrbl; disulfide bridge: Cys2-Cys7) (SEQ ID NO/35), eptifibatide (INTEGRILIN), calcitonin generelated peptide (CGRP) (Ala-Cys-Asp-Thr-Ala-Thr-Cys-Val-Thr-His-Arg-Leu-Ala-Gly-Leu-Leu-Ser-Arg-Ser-Gly-Gly-Val-Val-Lys-Ash-Asn-Phe-Val-Pro-Thr-Asn-Val-Gly-Ser-Lys-Ala-Phe-NH2; Disulfide bridge: Cys2-Cys7) (SEQ ID NO. 36), endomorphin-1 Tyr-Pro-Trp-Phe-NH2 (SEQ ID NO. 37); endomorphin-2 Tyr-Pro-Phe-Phe-NH2 (SEQ ID NO. 38), nociceptin (also known as Orphanin FQ, Phe-Gly-Gly-Phe-Thr-Gly-Ala-Arg-Lys-Ser-Ala-Arg-Lys-Leu-Ala-Asn-Gln) (SEQ ID NO. 39), angiotensinogen (1-13) (Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His) (SEQ ID NO. 40) adrenomodullin (1-12) (Tyr-Arg-Gln-Ser-Met-Asn-Asn-Phe-Gln-Gly-Leu-Arg) (SEQ ID NO./41), antiarrhytmic peptide (AAP) (Gly-Pro-Hyp-Gly-Ala-Gly) (SEQ ID NO. 42), Antagonist G (Arg-DTrp-(nMe)Phe-DTrp-Leu-Met-NH2), indolicidin (Ile-Leu-Pro-Trp-Lys-Trp-Pro-Trp-Pro-Trp-Arg-Arg-NH2) (SEQ ID NO. 43), osteocalcin (37-49) (Gly-Phe-Gln-Glu-Ala-Tyr-Arg-Arg-Phe-Tyr-Gly-Pro-Val) (SEQ ID NO. 44), cortistatin 29 (1-13) (Glp-Glu-Arg-Pro-Pro-Leu-Gln-Gln-Pro-Pro-His-Arg-Asp) (SEQ ID NO. 45), cortistatin 14 Pro-Cys-Lys-Asn-Phe-Phe-Trp-Lys-Thr-Phe-Ser-Ser-Cys-Lys; Disulfide

SUPPLY

K X

bridge: Cys2-Cys13 (SEQ ID NO. 46), PD-145065 (Ac-D-Bhg-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO. 47), PD-142893 (Ac-D-Dip-Leu-Asp-Ile-Ile-Trp) (SEQ ID NO. 48), fibrinogen binding inhibitor peptide (His-His-Leu-Gly-Gly-Ala-Lys-Gln-Ala-Gly-Asp-Val) (SEQ ID NO. 49), leptin (93-105) (Asn-Val-Ile-Gln-Ile-Ser-Asn-Asp-Leu-Glu-Asn-Leu-Arg) (SEQ ID NO. 50), GR 83074 (Boc-Arg-Ala-DTrp-Phe-DPro-Pro-Nle-NH2) (SEQ ID NO. 51), Tyr-W-MIF-1 (Tyr-Pro-Trp-Gly-NH2) (SEQ ID NO. 52), parathyroid hormone related peptide (107-111) (Thr-Arg-Ser-Ala-Trp) (SEQ ID NO. 53), angiotensinogen (1-14) Asp-Arg-Val-Tyr-Ile-His-Pro-Phe-His-Leu-Val-Ile-His-Asn (SEQ ID NO. 54), Leupeptin (Ac-Leu-Leu-Arg-CHO), sandostatin and any modified or truncated analogue thereof.

25. (amended) A peptide conjugate according to claim 1 wherein the conjugate is

H-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Gln-Asp-Ile-Met-Ser Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu-Lys6-NH2 (GHRH(1-44)(Human)-Lys6-NH2) (SEQ ID NO. 88);

H-Tyr-Ala-Asp-Ala-Ile-Phe-Thr-Asn-Ser-Tyr-Arg-Lys-Val-Leu-Gly-Gln-Leu-Ser-Ala-Arg-Lys-Leu-Leu-Gln-Asp-Ile-Met-Ser Arg-Gln-Gln-Gly-Glu-Ser-Asn-Gln-Glu-Arg-Gly-Ala-Arg-Ala-Arg-Leu-Glu6-NH2 (GHRH (1-44)(Human)-Glu6-NH2) (SEQ ID NO. 89);

H- Lys6-Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys-His-Leu-Asn-Ser-Met-Glu-Arg-Val-Glu-Trp-Leu-Arg-Lys-Lys-Leu-Gln-Asp-Val-His-Asn-Phe-OH (Lys6-PTH(1-34)(Human)-OH) (SEQ ID NO. 90);

H-Ser-Val-Ser-Glu-Ile-Gln-Leu-Met-His-Asn-Leu-Gly-Lys-His-Leu-Asn-Ser-Met-Glu-Arg-Val-Glu-Trp-Leu-Arg-Lys-Lys-Leu-Gln-Asp-Val-His-Asn-Phe-Lys6-OH (PTH(1-34)(Human)-Lys6-OH) (SEQ ID NO. 91);



H-His-Ala-Glu-Gly-Thr-Phe-Thr-Ser-Asp-Val-Ser-Ser-Tyr-Leu-Glu-Gly-Gln-Ala-Ala-Lys-Glu-Phe-Ile-Ala-Trp-Leu-Val-Lys-Gly-Arg-Lys6-OH (GLP-1-(7-36)(Human)-Lys6-OH) (SEQ ID NO. 92);

H-Gly-Gly-Thr-Tyr-Ser-Cys(Acm)-His-Phe-Gly-Pro-Leu-Thr-Trp-Val-Cys(Acm)-Lys-Pro-Gln-Gly-Gly-Lys6-OH (EMP-1-Lys6-OH) (SEQ ID NO. 93);

H-Lys6-Gly-Gly-Thr-Tyr-Ser-Cys(Acm)-His-Phe-Gly-Pro-Leu-Thr-Trp-Val-Cys(Acm)-Lys-Pro-Gln-Gly-Gly-OH (Lys6-EMP-1-OH) (SEQ ID NO. 94);

H-Lys6-Gly-Gly-Thr-Tyr-Ser-Cys(Acm)-His-Phe-Gly-Pro-Leu-Thr-Trp-Val-Cys(Acm)-Lys-Pro-Gln-Gly-Gly-Lys6-OH (Lys6-EMP-1-Lys6-OH) (SEQ ID NO. 95);

H-Aib-His-2-D-Nal-D-Phe-Lys-(Lys)6-NH2 (GHRP-(Lys)6-NH2) (SEQ ID NO. 96);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Lys-Glu-Glu-Glu-Lys-OH (Leu-enkephalin-Lys-Lys-Glu-Glu-Glu-Lys-OH) (SEQ ID NO. 97);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Glu-Glu-Glu-Glu-Lys-OH (Leu-enkephalin-Lys-Glu-Glu-Glu-Glu-Glu-Lys-OH) (SEQ ID NO. 98);

H-Tyr-Gly-Gly-Phe-Leu-Lys-Glu-Glu-Glu-Glu-Lys--OH (Leu-enkephalin-(Lys-Glu)3 (SEQ ID NO. 99);

H-Tyr-Gly-Gly-Phe-Leu-(Dapa)6-OH (Leu-enkephalin-(Dapa)6-OH) (SEQ ID NO. 100);

H-Lys6-Tyr-Gly-Gly-Phe-Leu-OH (H-Lys6-Leu-enkephalin) (SEQ ID NO. 101);

H-Tyr-Gly-Gly-Phe-Leu- Lys6-OH (H-Leu-enkephalin-Lys6) (SEQ ID NO. 11);